

ABSTRACT: Adhesion of lymphocytes to endothelium is vital to lymphocyte migration into lymphoid tissue and into inflammatory sites. In this review, Yoji Shimizu and colleagues identify the molecules that mediate lymphocyte-endothelial cell adhesion, describe the underlying principles of lymphocyte migration, and discuss a model of the sequence of events that allow a lymphocyte to successfully attach to endothelium and migrate into the surrounding tissue.

Set	Items	Description
S1	3	DENDRITIC (5N) (P(W)SELECTIN)
S2	1	RD (unique items)
S3	231	DENDRITIC? (S) SELECTIN
S4	154	S3 NOT PY>1999
S5	4	S4 AND (VECTOR? OR RETROVIR? OR PLASMID? OR ADENOVIR? OR D-NA)
S6	3	RD (unique items)
S7	150	S4 NOT S5
S8	9	S7 AND PLATELET?
S9	6	S8 NOT S1
S10	3	RD (unique items)
S11	48	(CD62 OR CD62? OR ((E OR L OR P)(W)SELECTIN)) (6N) DENDRIT-IC
S12	35	S11 NOT PY>1999
S13	23	RD (unique items)
S14	0	S13 (S) (VECTOR? OR PLASMID? OR DNA OR RETROVIR? OR ADENOV-IR?)
S15	135	PLATELET? (5N) DENDRITIC
S16	110	S15 NOT PY>1999
S17	55	RD (unique items)
S18	17	S17 AND (ACTIVAT? (4N) PLATELET?)
S19	451	(CD62 OR CD62? OR ((E OR L OR P)(W)SELECTIN)) (5N) (VECTOR? OR PLASMID? OR DNA OR RETROVIR? OR ADENOVIR?)
S20	344	S19 NOT PY>1999
S21	0	S20 AND DENDRITIC
S22	344	S20 NOT (S5 OR S10 OR S13 OR S17)
S23	116	S22 AND (TRANSFECT? OR TRANSDUC?)
S24	64	RD (unique items)
S25	38	S17 NOT S18
S26	38	RD (unique items)
S27	4207	(SELECTIN? OR CD62?) (S) REVIEW?
S28	24	(SELECTIN OR ((P OR L OR E)(W)SELECTIN)) (4N) REVIEW?
S29	13606	RD
S30	24	S28
S31	11	RD (unique items)
?		

4/1/99 -
priority

platelets (ABSTRACT AVAILABLE)

Author(s): Escolar G (REPRINT) ; Rao GH; Nieuwenhuis HK; White JG
Corporate Source: UNIV BARCELONA, HOSP CLIN, SERV HEMOTERAPIA & HEMOSTASIA,
VILLARROEL 170/E-08036 BARCELONA//SPAIN/ (REPRINT); UNIV
MINNESOTA, /MINNEAPOLIS//MN/55455; UNIV UTRECHT
HOSP, /UTRECHT//NETHERLANDS/

Journal: PLATELETS, 1996, V7, N5-6, P297-301

ISSN: 0953-7104 Publication date: 19960000

Publisher: CARFAX PUBL CO, PO BOX 25, ABINGDON, OXFORDSHIRE, ENGLAND OX14
3UE

Language: English Document Type: ARTICLE

Abstract: P-selectin is an alpha granule membrane associated glycoprotein in platelets (P1) expressed on the surface following exposure to secretagogues in suspension. It is not clear, whether P-selectin is transported from granule membranes to the P1 surface, or released by surface-activation (SfA). In the present study washed P1 were allowed to interact with grids for different periods of time (5-20 min), fixed briefly and exposed to a monoclonal antibody to P-selectin. Grids were washed and exposed to goat anti-mouse IgG antibody coupled to 10 nm gold particles. Examination in the electron microscope revealed a differential distribution of the gold probe on SfA P1. Discoid P1 did not express P-selectin. Early dendritic P1 revealed a few gold probes for P-selectin near the central zone, Late dendritic P1 expressed P-selectin on P1 bodies and some on pseudopods. On fully spread P1 P-selectin probes were evenly distributed, but more concentrated on the peripheral margin than the central zone. Results demonstrate that P-selectin is released from SfA P1. Its initial expression in the central zone suggests it reaches the surface through channels of the open canalicular system. The centrifugal movement of P-selectin is opposite in direction to translocation of mobile receptor-ligand complexes.

13/3, AB/22 (Item 9 from file: 34)

DIALOG(R) File 34: SciSearch(R) Cited Ref Sci

(c) 2001 Inst for Sci Info. All rts. reserv.

02706439 Genuine Article#: LY104 Number of References: 0

Title: E- SELECTIN DEPENDENT IN-VITRO ADHESION OF BLOOD DENDRITIC
CELLS TO HUMAN UMBILICAL-CORD ENDOTHELIAL-CELLS

Author(s): SRINIVAS U; LARSSON M; LUNDBLAD A; FORSUM U

Corporate Source: FAC HLTH SCI LINKOPING, DEPT CLIN CHEM/S-58185

LINKOPING//SWEDEN/; FAC HLTH SCI LINKOPING, DEPT CLIN MICROBIOL/S-58185

LINKOPING//SWEDEN/

Journal: GLYCOCONJUGATE JOURNAL, 1993, V10, N4 (AUG), P268

ISSN: 0282-0080

Language: ENGLISH Document Type: MEETING ABSTRACT

P-selectin mediates the interaction of circulating leukocytes with platelets and microvascular endothelium in response to oxidized lipoprotein in vivo.

Lehr HA; Olofsson AM; Carew TE; Vajkoczy P; von Andrian UH; Hubner C;
Berndt MC; Steinberg D; Messmer K; Arfors KE

Institute for Surgical Research, University of Munich, Federal Republic of Germany.

Laboratory investigation (UNITED STATES) Sep 1994, 71 (3) p380-6,
ISSN 0023-6837 Journal Code: KZ4

Contract/Grant No.: HL46022, HL, NHLBI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

BACKGROUND: Oxidized low density lipoprotein (oxLDL) has been demonstrated to stimulate leukocyte/endothelium interaction, an early feature of atherogenesis. Using the skinfold chamber model for intravital microscopy in hamsters and mice, we have shown that oxLDL-induced leukocyte adhesion to microvascular endothelium shares many characteristics with leukocyte adhesion during inflammation and ischemia/reperfusion, including

probably not
Adams?

EB1 12 1

the involvement of beta 2 integrin adhesion molecules. In light of the two-step model of leukocyte adhesion, we have examined the contribution of P-selectin to oxLDL-induced leukocyte/endothelium interaction. P-selectin is an inducible adhesion molecule on platelets and endothelium, mediating the initial steps of leukocyte margination and rolling along the endothelial lining, as well as of aggregate formation between platelets and leukocytes. EXPERIMENTAL DESIGN: For our studies, we used the dorsal skinfold chamber model for intravital fluorescence microscopy on awake Syrian golden hamsters. Hamsters were treated 10 minutes before oxLDL-injection (oxidized by Cu2+, 4 mg/kg body weight, intravenously) with blocking antibodies to P-selectin (2 mg/kg body weight intravenously, N = 7). RESULTS: In seven control animals (pretreated with an irrelevant IgG antibody), oxLDL injection elicited leukocyte rolling and adhesion on both venular and arteriolar endothelium, and also the formation of aggregates tumbling down the microvessels and firmly adhering to the microvascular endothelium. The aggregates consisted of leukocytes and **activated, dendritic platelets**, as assessed by scanning electron microscopy of the buffy coat isolated by density gradient centrifugation of whole blood taken from hamsters 15 minutes after injection of oxLDL. Leukocyte adhesion to venular and arteriolar endothelium, as well as the formation of leukocyte/platelet aggregates were significantly reduced by pretreatment of the animals with anti-P-selectin antibodies. CONCLUSIONS: These data emphasize the similarities between leukocyte adhesion in response to oxLDL and in other pathophysiologic conditions, identifying P-selectin as a crucial player in the interaction between leukocytes and microvascular endothelium as well as in the formation of circulating leukocyte/platelet aggregates.

08335129 Genuine Article#: 257PH Number of References: 0

Title: Activated platelets mediate CD40 independent maturation of dendritic cells.

Author(s): Marolleau JP; Zini JM; Lacassagne MN; Ternaux B; Garcon L; Zitvogel L; Benbunan M

Corporate Source: HOP ST LOUIS, BLOOD BANK, ILF/PARIS//FRANCE/

Journal: BLOOD, 1999, V94, N10, 1, 1 (NOV 15), P938-938

ISSN: 0006-4971 Publication date: 19991115

Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE 300, WASHINGTON, DC 20036-2422

Language: English Document Type: MEETING ABSTRACT

18/3, AB/12 (Item 2 from file: 34)

DIALOG(R) File 34: SciSearch(R) Cited Ref Sci

(c) 2001 Inst for Sci Info. All rts. reserv.

07136151 Genuine Article#: 126TN Number of References: 1

Title: Anti-phospholipid antibodies opsonize activated platelets for uptake by dendritic cells: relevance to epitope spreading in platelet autoimmunity.

Author(s): Bondanza A; Pellegatta F; Zimmermann VS; Balestrieri G; Tincani A; Sabbadini MG; Manfredi AA; Rovere P

Corporate Source: HOSP SAN RAFFAELE, /I-20132 MILAN//ITALY//; SPEDALI CIVIL BRESCIA, /I-25125 BRESCIA//ITALY//; CIML, /MARSEILLE//FRANCE/

Journal: JOURNAL OF LEUKOCYTE BIOLOGY, 1998, 2, PF17-F17

ISSN: 0741-5400 Publication date: 19980000

Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998

Language: English Document Type: MEETING ABSTRACT

Divergent fates of P- and E-selectins after their expression on the plasma membrane.

Subramaniam M; Koedam JA; Wagner DD

Department of Medicine, New England Medical Center, Boston, Massachusetts.

Molecular biology of the cell (UNITED STATES) Aug 1993, 4 (8) p791-801, ISSN 1059-1524 Journal Code: BAU

Contract/Grant No.: P01 HL42443, HL, NHLBI; R01 HL41002, HL, NHLBI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

P-selectin and E-selectin are related adhesion receptors for monocytes and neutrophils that are expressed by stimulated endothelial cells. P-selectin is stored in Weibel-Palade bodies, and it reaches the plasma membrane after exocytosis of these granules. E-selectin is not stored, and its synthesis is induced by cytokines. We studied the fate of the two proteins after their surface expression by following the intracellular routing of internalized antibodies to the selectins. By immunofluorescent staining, P-selectin antibody was first seen in endosomes, then in the Golgi region, and finally in Weibel-Palade bodies. In contrast, the E-selectin antibody was detected only in endosomes and lysosomes. Subcellular fractionation of cells after 4 h chase confirmed the localization of P-selectin antibody in storage granules and of the E-selectin antibody in lysosomes. In AtT-20 cells, a mouse pituitary cell line, **transfected** with P- or E-selectin, only P-selectin was delivered to the endogenous adrenocorticotrophic hormone storage granules after endocytosis. Deletion of the cytoplasmic domain abolished internalization. In summary, after a brief surface exposure, internalized E-selectin is degraded in the lysosomes, whereas P-selectin returns to the storage granules from where it can be reused.

STRUCTURE AND FUNCTION OF L SELECTIN REVIEW ARTICLE

AUTHOR: KANSAS G S

AUTHOR ADDRESS: DEP. PATHOL., HARVARD MED. SCH., BOSTON, MASS.

JOURNAL: APMIS (ACTA PATHOL MICROBIOL IMMUNOL SCAND) 100 (4). 1992.

287-293. 1992

FULL JOURNAL NAME: APMIS (Acta Pathologica Microbiologica et Immunologica Scandinavica)

CODEN: APMSE

DOCUMENT TYPE: Review

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: The selectins are a newly described family of carbohydrate-binding adhesion molecules involved in the regulation of leukocyte traffic. Selectins are composed of an N-terminal C-type lectin domain, a single EGF domain, a variable number of short consensus repeat (SCR) domains, a transmembrane region and a cytoplasmic tail. L-selectin (LAM-1/LECAM-1/LECCAM-1) is the only selectin expressed on leukocytes, and mediates a number of leukocyte-endothelial interactions, including the binding of lymphocytes to HEV of peripheral lymph node high endothelial venules (HEV), neutrophil rolling, and leukocyte attachment to cytokine-treated endothelium in vitro. Stable transfectants expressing a series of chimeric selectins and deletion mutants were functionally analyzed in order to determine the molecular basis of adhesion mediated by L-selectin. The specificity of adhesion was found to reside entirely within the lectin domain, suggesting that this domain is the only domain of the protein to interact with the carbohydrate ligand. These results make previous observations that certain mAbs which block function map to each of the extracellular domains difficult to interpret. In addition, deletion of the cytoplasmic tail of L-selectin abolished adhesion, without affecting ligand recognition. Thus, each domain of the selectins has an important, but distinct, role in cell adhesion.

LYMPHOCYTE INTERACTIONS WITH ENDOTHELIAL CELLS

AUTHOR: SHIMIZU Y; NEWMAN W; TANAKA Y; SHAW S

AUTHOR ADDRESS: DEP. MICROBIOL. AND IMMUNOL., UNIV. MICH. MED. SCH., ANN ARBOR, MICH. 48109.

JOURNAL: IMMUNOL TODAY 13 (3). 1992. 106-112. 1992

FULL JOURNAL NAME: Immunology Today

CODEN: IMTOD

DOCUMENT TYPE: Review

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

Title: Ultrastructural expression of P-selectin on surface activated platelets (ABSTRACT AVAILABLE)

Author(s): Escolar G (REPRINT) ; Rao GH; Nieuwenhuis HK; White JG
Corporate Source: UNIV BARCELONA, HOSP CLIN, SERV HEMOTERAPIA & HEMOSTASIA,
VILLARROEL 170/E-08036 BARCELONA//SPAIN/ (REPRINT); UNIV
MINNESOTA, /MINNEAPOLIS//MN/55455; UNIV UTRECHT
HOSP, /UTRECHT//NETHERLANDS/

Journal: PLATELETS, 1996, V7, N5-6, P297-301

ISSN: 0953-7104 Publication date: 19960000

Publisher: CARFAX PUBL CO, PO BOX 25, ABINGDON, OXFORDSHIRE, ENGLAND OX14
3UE

Language: English Document Type: ARTICLE

Abstract: P-selectin is an alpha granule membrane associated glycoprotein in platelets (Pl) expressed on the surface following exposure to secretagogues in suspension. It is not clear, whether P-selectin is transported from granule membranes to the Pl surface, or released by surface-activation (SfA). In the present study washed Pl were allowed to interact with grids for different periods of time (5-20 min), fixed briefly and exposed to a monoclonal antibody to P-selectin. Grids were washed and exposed to goat anti-mouse IgG antibody coupled to 10 nm gold particles. Examination in the electron microscope revealed a differential distribution of the gold probe on SfA Pl. Discoid Pl did not express **P-selectin**. Early **dendritic** Pl revealed a few gold probes for **P-selectin** near the central zone, Late **dendritic** Pl expressed **P-selectin** on Pl bodies and some on pseudopods. On fully spread Pl P-selectin probes were evenly distributed, but more concentrated on the peripheral margin than the central zone. Results demonstrate that P-selectin is released from SfA Pl. Its initial expression in the central zone suggests it reaches the surface through channels of the open canalicular system. The centrifugal movement of P-selectin is opposite in direction to translocation of mobile receptor-ligand complexes.

13/3,AB/3 (Item 3 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

09884319 98425544 PMID: 9754573

Lymphocyte triggering via L-selectin leads to enhanced galectin-3-mediated binding to dendritic cells.

Swarte VV; Mebius RE; Joziassse DH; Van den Eijnden DH; Kraal G
Department of Medical Chemistry, Vrije Universiteit, Amsterdam, The Netherlands.

European journal of immunology (GERMANY) Sep 1998, 28 (9) p2864-71,
ISSN 0014-2980 Journal Code: EN5

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

For proper immune surveillance, naive lymphocytes are recruited from the blood into secondary lymphoid organs. L-selectin expressed on lymphocytes plays an important role in the initial attachment of these cells to high endothelial venules (HEV) in lymph nodes. Previously, we found that triggering via L-selectin resulted in activation of lymphocytes, followed by an alteration in their adhesion capacity. This suggested that L-selectin triggering might play a role in cell-cell interactions after lymph node entry. Here, we identify a novel adhesion mechanism involving **L-selectin**-triggered lymphocytes and **dendritic** cells, and we show that enhanced binding to dendritic cells is mediated by galectin-3 and not by integrins. Furthermore, it was shown that L-selectin-triggered T lymphocytes exhibited enhanced proliferation in an allogeneic mixed lymphocyte reaction. It is concluded that, in addition to a role for L-selectin in tethering and rolling on endothelium, triggering of the molecule on the lymphocyte surface leads to changes that are pertinent for the function of the cell after passing the HEV. We argue that the described adhesion mechanism plays a role in optimizing the initial interaction between dendritic cells and lymphocytes.

05549069 Genuine Article#: WF799 Number of References: 37

Title: Ultrastructural expression of P-selectin on surface activated

Title: Ultrastructural expression of P-selectin on surface activated platelets (ABSTRACT AVAILABLE)

Author(s): Escolar G (REPRINT) ; Rao GH; Nieuwenhuis HK; White JG
Corporate Source: UNIV BARCELONA, HOSP CLIN, SERV HEMOTERAPIA & HEMOSTASIA,
VILLARROEL 170/E-08036 BARCELONA//SPAIN/ (REPRINT); UNIV
MINNESOTA, /MINNEAPOLIS//MN/55455; UNIV UTRECHT
HOSP, /UTRECHT//NETHERLANDS/

Journal: PLATELETS, 1996, V7, N5-6, P297-301

ISSN: 0953-7104 Publication date: 19960000

Publisher: CARFAX PUBL CO, PO BOX 25, ABINGDON, OXFORDSHIRE, ENGLAND OX14
3UE

Language: English Document Type: ARTICLE

Abstract: P-selectin is an alpha granule membrane associated glycoprotein in platelets (P1) expressed on the surface following exposure to secretagogues in suspension. It is not clear, whether P-selectin is transported from granule membranes to the P1 surface, or released by surface-activation (SfA). In the present study washed P1 were allowed to interact with grids for different periods of time (5-20 min), fixed briefly and exposed to a monoclonal antibody to P-selectin. Grids were washed and exposed to goat anti-mouse IgG antibody coupled to 10 nm gold particles. Examination in the electron microscope revealed a differential distribution of the gold probe on SfA P1. Discoid P1 did not express P-selectin. Early dendritic P1 revealed a few gold probes for P-selectin near the central zone, Late dendritic P1 expressed P-selectin on P1 bodies and some on pseudopods. On fully spread P1 P-selectin probes were evenly distributed, but more concentrated on the peripheral margin than the central zone. Results demonstrate that P-selectin is released from SfA P1. Its initial expression in the central zone suggests it reaches the surface through channels of the open canalicular system. The centrifugal movement of P-selectin is opposite in direction to translocation of mobile receptor-ligand complexes.

13/3, AB/3 (Item 3 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

09884319 98425544 PMID: 9754573

Lymphocyte triggering via L-selectin leads to enhanced galectin-3-mediated binding to dendritic cells.

Swarte VV; Mebius RE; Joziassse DH; Van den Eijnden DH; Kraal G

Department of Medical Chemistry, Vrije Universiteit, Amsterdam, The Netherlands.

European journal of immunology (GERMANY) Sep 1998, 28 (9) p2864-71,
ISSN 0014-2980 Journal Code: EN5

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

For proper immune surveillance, naive lymphocytes are recruited from the blood into secondary lymphoid organs. L-selectin expressed on lymphocytes plays an important role in the initial attachment of these cells to high endothelial venules (HEV) in lymph nodes. Previously, we found that triggering via L-selectin resulted in activation of lymphocytes, followed by an alteration in their adhesion capacity. This suggested that L-selectin triggering might play a role in cell-cell interactions after lymph node entry. Here, we identify a novel adhesion mechanism involving L-selectin-triggered lymphocytes and dendritic cells, and we show that enhanced binding to dendritic cells is mediated by galectin-3 and not by integrins. Furthermore, it was shown that L-selectin-triggered T lymphocytes exhibited enhanced proliferation in an allogeneic mixed lymphocyte reaction. It is concluded that, in addition to a role for L-selectin in tethering and rolling on endothelium, triggering of the molecule on the lymphocyte surface leads to changes that are pertinent for the function of the cell after passing the HEV. We argue that the described adhesion mechanism plays a role in optimizing the initial interaction between dendritic cells and lymphocytes.

05549069 Genuine Article#: WF799 Number of References: 37

Title: Ultrastructural expression of P-selectin on surface activated

platelets (ABSTRACT AVAILABLE)

Author(s): Escolar G (REPRINT) ; Rao GH; Nieuwenhuis HK; White JG
Corporate Source: UNIV BARCELONA, HOSP CLIN, SERV HEMOTERAPIA & HEMOSTASIA,
VILLARROEL 170/E-08036 BARCELONA//SPAIN/ (REPRINT); UNIV
MINNESOTA, /MINNEAPOLIS//MN/55455; UNIV UTRECHT
HOSP, /UTRECHT//NETHERLANDS/

Journal: PLATELETS, 1996, V7, N5-6, P297-301

ISSN: 0953-7104 Publication date: 19960000

Publisher: CARFAX PUBL CO, PO BOX 25, ABINGDON, OXFORDSHIRE, ENGLAND OX14
3UE

Language: English Document Type: ARTICLE

Abstract: P-selectin is an alpha granule membrane associated glycoprotein in platelets (P1) expressed on the surface following exposure to secretagogues in suspension. It is not clear, whether P-selectin is transported from granule membranes to the P1 surface, or released by surface-activation (SfA). In the present study washed P1 were allowed to interact with grids for different periods of time (5-20 min), fixed briefly and exposed to a monoclonal antibody to P-selectin. Grids were washed and exposed to goat anti-mouse IgG antibody coupled to 10 nm gold particles. Examination in the electron microscope revealed a differential distribution of the gold probe on SfA P1. Discoid P1 did not express P-selectin. Early dendritic P1 revealed a few gold probes for P-selectin near the central zone, Late dendritic P1 expressed P-selectin on P1 bodies and some on pseudopods. On fully spread P1 P-selectin probes were evenly distributed, but more concentrated on the peripheral margin than the central zone. Results demonstrate that P-selectin is released from SfA P1. Its initial expression in the central zone suggests it reaches the surface through channels of the open canalicular system. The centrifugal movement of P-selectin is opposite in direction to translocation of mobile receptor-ligand complexes.

13/3, AB/22 (Item 9 from file: 34)

DIALOG(R) File 34: SciSearch(R) Cited Ref Sci

(c) 2001 Inst for Sci Info. All rts. reserv.

02706439 Genuine Article#: LY104 Number of References: 0

Title: E- SELECTIN DEPENDENT IN-VITRO ADHESION OF BLOOD DENDRITIC
CELLS TO HUMAN UMBILICAL-CORD ENDOTHELIAL-CELLS

Author(s): SRINIVAS U; LARSSON M; LUNDBLAD A; FORSUM U

Corporate Source: FAC HLTH SCI LINKOPING, DEPT CLIN CHEM/S-58185

LINKOPING//SWEDEN/; FAC HLTH SCI LINKOPING, DEPT CLIN MICROBIOL/S-58185

LINKOPING//SWEDEN/

Journal: GLYCOCONJUGATE JOURNAL, 1993, V10, N4 (AUG), P268

ISSN: 0282-0080

Language: ENGLISH Document Type: MEETING ABSTRACT

P-selectin mediates the interaction of circulating leukocytes with platelets and microvascular endothelium in response to oxidized lipoprotein in vivo.

Lehr HA; Olofsson AM; Carew TE; Vajkoczy P; von Andrian UH; Hubner C;
Berndt MC; Steinberg D; Messmer K; Arfors KE

Institute for Surgical Research, University of Munich, Federal Republic of Germany.

Laboratory investigation (UNITED STATES) Sep 1994, 71 (3) p380-6,

ISSN 0023-6837 Journal Code: KZ4

Contract/Grant No.: HL46022, HL, NHLBI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

BACKGROUND: Oxidized low density lipoprotein (oxLDL) has been demonstrated to stimulate leukocyte/endothelium interaction, an early feature of atherogenesis. Using the skinfold chamber model for intravital microscopy in hamsters and mice, we have shown that oxLDL-induced leukocyte adhesion to microvascular endothelium shares many characteristics with leukocyte adhesion during inflammation and ischemia/reperfusion, including

the involvement of beta 2 integrin adhesion molecules. In light of the two-step model of leukocyte adhesion, we have examined the contribution of P-selectin to oxLDL-induced leukocyte/endothelium interaction. P-selectin is an inducible adhesion molecule on platelets and endothelium, mediating the initial steps of leukocyte margination and rolling along the endothelial lining, as well as of aggregate formation between platelets and leukocytes. **EXPERIMENTAL DESIGN:** For our studies, we used the dorsal skinfold chamber model for intravital fluorescence microscopy on awake Syrian golden hamsters. Hamsters were treated 10 minutes before oxLDL-injection (oxidized by Cu²⁺, 4 mg/kg body weight, intravenously) with blocking antibodies to P-selectin (2 mg/kg body weight intravenously, N = 7). **RESULTS:** In seven control animals (pretreated with an irrelevant IgG antibody), oxLDL injection elicited leukocyte rolling and adhesion on both venular and arteriolar endothelium, and also the formation of aggregates tumbling down the microvessels and firmly adhering to the microvascular endothelium. The aggregates consisted of leukocytes and **activated, dendritic platelets**, as assessed by scanning electron microscopy of the buffy coat isolated by density gradient centrifugation of whole blood taken from hamsters 15 minutes after injection of oxLDL. Leukocyte adhesion to venular and arteriolar endothelium, as well as the formation of leukocyte/platelet aggregates were significantly reduced by pretreatment of the animals with anti-P-selectin antibodies. **CONCLUSIONS:** These data emphasize the similarities between leukocyte adhesion in response to oxLDL and in other pathophysiologic conditions, identifying P-selectin as a crucial player in the interaction between leukocytes and microvascular endothelium as well as in the formation of circulating leukocyte/platelet aggregates.

08335129 Genuine Article#: 257PH Number of References: 0

Title: Activated platelets mediate CD40 independent maturation of dendritic cells.

Author(s): Marolleau JP; Zini JM; Lacassagne MN; Ternaux B; Garcon L; Zitvogel L; Benbunan M

Corporate Source: HOP ST LOUIS, BLOOD BANK, ILF/PARIS//FRANCE/

Journal: BLOOD, 1999, V94, N10,1,1 (NOV 15), P938-938

ISSN: 0006-4971 **Publication date:** 19991115

Publisher: AMER SOC HEMATOLOGY, 1200 19TH ST, NW, STE 300, WASHINGTON, DC 20036-2422

Language: English **Document Type:** MEETING ABSTRACT

18/3,AB/12 (Item 2 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

(c) 2001 Inst for Sci Info. All rts. reserv.

07136151 Genuine Article#: 126TN Number of References: 1

Title: Anti-phospholipid antibodies opsonize activated platelets for uptake by dendritic cells: relevance to epitope spreading in platelet autoimmunity.

Author(s): Bondanza A; Pellegatta F; Zimmermann VS; Balestrieri G; Tincani A; Sabbadini MG; Manfredi AA; Rovere P

Corporate Source: HOSP SAN RAFFAELE, /I-20132 MILAN//ITALY//; SPEDALI CIVIL BRESCIA, /I-25125 BRESCIA//ITALY//; CIML, /MARSEILLE//FRANCE/

Journal: JOURNAL OF LEUKOCYTE BIOLOGY, 1998, 2, PF17-F17

ISSN: 0741-5400 **Publication date:** 19980000

Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998

Language: English **Document Type:** MEETING ABSTRACT

Divergent fates of P- and E-selectins after their expression on the plasma membrane.

Subramaniam M; Koedam JA; Wagner DD
Department of Medicine, New England Medical Center, Boston, Massachusetts.

Molecular biology of the cell (UNITED STATES) Aug 1993, 4 (8)
p791-801, ISSN 1059-1524 Journal Code: BAU

Contract/Grant No.: P01 HL42443, HL, NHLBI; R01 HL41002, HL, NHLBI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

P-selectin and E-selectin are related adhesion receptors for monocytes and neutrophils that are expressed by stimulated endothelial cells. P-selectin is stored in Weibel-Palade bodies, and it reaches the plasma membrane after exocytosis of these granules. E-selectin is not stored, and its synthesis is induced by cytokines. We studied the fate of the two proteins after their surface expression by following the intracellular routing of internalized antibodies to the selectins. By immunofluorescent staining, P-selectin antibody was first seen in endosomes, then in the Golgi region, and finally in Weibel-Palade bodies. In contrast, the E-selectin antibody was detected only in endosomes and lysosomes. Subcellular fractionation of cells after 4 h chase confirmed the localization of P-selectin antibody in storage granules and of the E-selectin antibody in lysosomes. In AtT-20 cells, a mouse pituitary cell line, **transfected** with P- or E-selectin, only P-selectin was delivered to the endogenous adrenocorticotrophic hormone storage granules after endocytosis. Deletion of the cytoplasmic domain abolished internalization. In summary, after a brief surface exposure, internalized E-selectin is degraded in the lysosomes, whereas P-selectin returns to the storage granules from where it can be reused.

STRUCTURE AND FUNCTION OF L SELECTIN REVIEW ARTICLE

AUTHOR: KANSAS G S

AUTHOR ADDRESS: DEP. PATHOL., HARVARD MED. SCH., BOSTON, MASS.

JOURNAL: APMIS (ACTA PATHOL MICROBIOL IMMUNOL SCAND) 100 (4). 1992.
287-293. 1992

FULL JOURNAL NAME: APMIS (Acta Pathologica Microbiologica et Immunologica Scandinavica)

CODEN: APMSE

DOCUMENT TYPE: Review

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: The selectins are a newly described family of carbohydrate-binding adhesion molecules involved in the regulation of leukocyte traffic. Selectins are composed of an N-terminal C-type lectin domain, a single EGF domain, a variable number of short consensus repeat (SCR) domains, a transmembrane region and a cytoplasmic tail. L-selectin (LAM-1/LECAM-1/LECCAM-1) is the only selectin expressed on leukocytes, and mediates a number of leukocyte-endothelial interactions, including the binding of lymphocytes to HEV of peripheral lymph node high endothelial venules (HEV), neutrophil rolling, and leukocyte attachment to cytokine-treated endothelium in vitro. Stable transfectants expressing a series of chimeric selectins and deletion mutants were functionally analyzed in order to determine the molecular basis of adhesion mediated by L-selectin. The specificity of adhesion was found to reside entirely within the lectin domain, suggesting that this domain is the only domain of the protein to interact with the carbohydrate ligand. These results make previous observations that certain mAbs which block function map to each of the extracellular domains difficult to interpret. In addition, deletion of the cytoplasmic tail of L-selectin abolished adhesion, without affecting ligand recognition. Thus, each domain of the selectins has an important, but distinct, role in cell adhesion.

LYMPHOCYTE INTERACTIONS WITH ENDOTHELIAL CELLS

AUTHOR: SHIMIZU Y; NEWMAN W; TANAKA Y; SHAW S

AUTHOR ADDRESS: DEP. MICROBIOL. AND IMMUNOL., UNIV. MICH. MED. SCH., ANN ARBOR, MICH. 48109.

JOURNAL: IMMUNOL TODAY 13 (3). 1992. 106-112. 1992

FULL JOURNAL NAME: Immunology Today

CODEN: IMTOD

DOCUMENT TYPE: Review

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

Mechanisms that regulate the function of the selectins and their ligands.

Vestweber D; Blanks JE

Institute of Cell Biology, Center of Molecular Biology of Inflammation,
University of Munster, Munster, Germany.

Physiological reviews (UNITED STATES) Jan 1999, 79 (1) p181-213,
ISSN 0031-9333 Journal Code: P7M

Erratum in Physiol Rev 2000 Jul;80(3) followi

Languages: ENGLISH

Document type: Journal Article; Review; Review, Academic

Record type: Completed

Selectins are a family of three cell adhesion molecules (L-, E-, and P-selectin) specialized in capturing leukocytes from the bloodstream to the blood vessel wall. This initial cell contact is followed by the selectin-mediated rolling of leukocytes on the endothelial cell surface. This represents the first step in a cascade of molecular interactions that lead to leukocyte extravasation, enabling the processes of lymphocyte recirculation and leukocyte migration into inflamed tissue. The central importance of the selectins in these processes has been well documented in vivo by the use of adhesion-blocking antibodies as well as by studies on **selectin** gene-deficient mice. This **review** focuses on the molecular mechanisms that regulate expression and function(s) of the selectins and their ligands. Cell-surface expression of the selectins is regulated by a variety of different mechanisms. The selectins bind to carbohydrate structures on glycoproteins, glycolipids, and proteoglycans. Glycoproteins are the most likely candidates for physiologically relevant ligands. Only a few glycoproteins are appropriately glycosylated to allow strong binding to the selectins. Recently, more knowledge about the structure and the regulated expression of some of the carbohydrates on these ligands necessary for selectin binding has been accumulated. For at least one of these ligands, the physiological function is now well established. A novel and exciting aspect is the signaling function of the selectins and their ligands. Especially in the last two years, convincing data have been published supporting the idea that selectins and glycoprotein ligands of the selectins participate in the activation of leukocyte integrins.

PRINTED